

Amendments to the Claims:

1. (Currently amended) ~~A method for preparing an injectable formulation of pharmaceutical composition comprising~~ interferon-beta (IFN- $\beta$ ), wherein said composition is prepared by a method comprising the steps of:

- a) preparing a first solution comprising IFN- $\beta$ , isolating a pool of purified IFN- $\beta$  from this solution, and precipitating said IFN- $\beta$  from this pool using an alcohol to form a precipitate;
  - b) dissolving said precipitate in guanidine hydrochloride (HCl) to form a second solution comprising resolubilized denatured IFN- $\beta$  and guanidine HCl;
  - c) diluting said second solution into a first buffer to obtain a third solution comprising resolubilized renatured IFN-beta and residual guanidine HCl; and
  - d) removing residual guanidine HCl from said third solution by diafiltration or dialysis of said third solution into a second buffer that is pharmaceutically acceptable;
- ~~whereby said injectable formulation of IFN- $\beta$  is prepared.~~

2. (Currently amended) ~~A~~ The pharmaceutical composition comprising of claim 1, wherein said composition comprises substantially monomeric IFN- $\beta$  ~~produced by the method of claim 1.~~

3. (Currently amended) ~~The method~~ pharmaceutical composition of claim 1, wherein said second buffer contains arginine or sodium chloride.

4. (Currently amended) ~~The method~~ pharmaceutical composition of claim 1, wherein said first buffer has a pH of about 5.0 to about 8.0, and wherein said residual guanidine HCl is present in said third solution at a concentration of 1.6 M or less.

5. (Currently amended) ~~A method for preparing an injectable formulation of pharmaceutical composition comprising~~ interferon-beta (IFN- $\beta$ ), said method wherein said composition is prepared by a method comprising the steps of:

a) ~~\_\_\_\_\_denaturation of denaturing~~ IFN- $\beta$  with guanidine hydrochloride (HCl) followed by;  
b) ~~\_\_\_\_\_renaturation of renaturing~~ the IFN- $\beta$  via dilution into a first buffer to obtain a renatured IFN- $\beta$  solution comprising residual guanidine HCl[,]; and  
c) ~~\_\_\_\_\_~~ removing said residual guanidine HCl from said renatured IFN- $\beta$  solution by diafiltration or dialysis of said renatured IFN- $\beta$  solution into a second buffer that is pharmaceutically acceptable;  
~~whereby said injectable formulation of IFN- $\beta$  is prepared.~~

6. (Currently amended) The ~~method~~pharmaceutical composition of claim 5, wherein said first buffer has a pH of about 3.0 to about 5.0, and wherein said residual guanidine HCl is present in said renatured IFN- $\beta$  solution at a concentration of 1.6 M or less.

7. (Currently amended) The ~~method~~pharmaceutical composition of claim 6, wherein said first buffer has a pH of about 3.0 to about 4.0, and wherein said residual guanidine HCl is present in said renatured IFN- $\beta$  solution at a concentration of 0.2 M or less.

8. (Currently amended) The ~~method~~pharmaceutical composition of claim 7, wherein said first buffer has a pH of about 3.0, and wherein said residual guanidine HCl is present in said renatured IFN- $\beta$  solution at a concentration of 0.1 M or less.

9. (Currently amended) ~~A~~The pharmaceutical composition of claim 5, wherein said composition comprising comprises substantially monomeric IFN- $\beta$  ~~produced by the method of claim 5.~~

10. (Currently amended) A ~~method for preparing a~~ composition comprising substantially monomeric interferon-beta (IFN- $\beta$ ), wherein said composition is prepared by a said method comprising the steps of:

a) preparing a precipitate of substantially purified IFN- $\beta$ ;

- b) dissolving said precipitate in guanidine hydrochloride (HCl) to obtain a first solution comprising resolubilized denatured IFN- $\beta$ ; and
- c) renaturing said IFN- $\beta$  by dilution of said first solution with a buffer solution.

11. (Currently amended) The ~~method~~ composition of claim 10, wherein said buffer solution has a pH of about 5.0 to about 8.0.

12. (Currently amended) A pharmaceutical composition comprising ~~substantially monomeric IFN- $\beta$  produced by the method~~ the composition of claim 10.

13. (Currently amended) A ~~method for preparing an injectable formulation of~~ pharmaceutical composition comprising interferon-beta (IFN- $\beta$ ), wherein said method comprising composition is prepared by a method comprising the steps of:

- a) obtaining a sample comprising substantially purified IFN- $\beta$ ;
  - b) mixing said sample with guanidine hydrochloride (HCl) to obtain a first solution comprising solubilized denatured IFN- $\beta$ ;
  - c) diluting said first solution into a first buffer to obtain a second solution comprising solubilized renatured IFN-beta and residual guanidine HCl; and
  - d) removing residual guanidine HCl from said second solution by diafiltration or dialysis of said second solution into a second buffer that is pharmaceutically acceptable;
- ~~whereby said injectable formulation of IFN- $\beta$  is prepared.~~

14. (Currently amended) A ~~The~~ pharmaceutical composition comprising of claim 13, wherein said composition comprises substantially monomeric IFN- $\beta$  ~~produced by the method of~~ claim 13.

15. (Currently amended) The ~~method~~pharmaceutical composition of claim 13, wherein said first buffer has a pH of about 3.0 to about 5.0, and wherein said residual guanidine HCl is present in said second solution at a concentration of 1.6 M or less.

16. (Currently amended) The ~~method~~pharmaceutical composition of claim 15, wherein said first buffer has a pH of about 3.0 to about 4.0, and wherein said residual guanidine HCl is present in said second solution at a concentration of 0.2 M or less.

17. (Currently amended) The ~~method~~pharmaceutical composition of claim 16, wherein said first buffer has a pH of about 3.0, and wherein said residual guanidine HCl is present in said ~~renatured IFN- $\beta$~~ second solution at a concentration of 0.1 M or less.

18. (Currently amended) A ~~method for preparing a~~ composition comprising substantially monomeric interferon-beta (IFN- $\beta$ ), wherein said ~~method comprising composition is prepared by a method comprising the steps of:~~

- a) preparing a sample comprising substantially purified IFN- $\beta$ ;
- b) mixing said sample with guanidine hydrochloride (HCl) to obtain a first solution comprising solubilized denatured IFN- $\beta$ ; and
- c) renaturing said IFN- $\beta$  by dilution of said first solution with a buffer solution.

19. (Currently amended) The ~~method~~composition of claim 18, wherein said buffer solution has a pH of about 3.0 to about 5.0.

20. (Currently amended) A pharmaceutical composition comprising ~~substantially monomeric IFN- $\beta$  produced by the method~~the composition of claim 18.

21. (New) The pharmaceutical composition of claim 1, wherein said IFN- $\beta$  has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

22. (New) The pharmaceutical composition of claim 1, wherein said IFN- $\beta$  is glycosylated or unglycosylated.

23. (New) The pharmaceutical composition of claim 1, wherein said IFN- $\beta$  is recombinantly produced.

24. (New) The pharmaceutical composition of claim 1, wherein said IFN- $\beta$  has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

25. (New) The pharmaceutical composition of claim 1, wherein said composition is injectable.

26. (New) The pharmaceutical composition of claim 5, wherein said IFN- $\beta$  has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

27. (New) The pharmaceutical composition of claim 5, wherein said IFN- $\beta$  is glycosylated or unglycosylated.

28. (New) The pharmaceutical composition of claim 5, wherein said IFN- $\beta$  is recombinantly produced.

29. (New) The pharmaceutical composition of claim 5, wherein said IFN- $\beta$  has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

30. (New) The pharmaceutical composition of claim 5, wherein said composition is injectable.

31. (New) The pharmaceutical composition of claim 13, wherein said IFN- $\beta$  has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

32. (New) The pharmaceutical composition of claim 13, wherein said IFN- $\beta$  is glycosylated or unglycosylated.

33. (New) The pharmaceutical composition of claim 13, wherein said IFN- $\beta$  is recombinantly produced.

34. (New) The pharmaceutical composition of claim 13, wherein said IFN- $\beta$  has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

35. (New) The pharmaceutical composition of claim 13, wherein said composition is injectable.